REMARKS

Claims 2-4, 6, 8, 10, 12, 14, 16, 18-20, 22, 24-28, 30-37, and 39-50 have been cancelled. Claims 1 and 38 have been amended. New claims 51 and 52 are added. Claims 1, 5, 7, 9, 11, 13, 15, 17, 21, 23, 29, 38, 51 and 52 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Applicants would like to thank the Examiner for the courteous interview conducted on January 3, 2005. The substance of that interview is presented on page 5.

Rejection under 35 U.S.C. § 103(a)

Claims 1, 3, 19-24, 29-37, 39-45, and 47-50 are rejected under 35 U.S.C. § 103 (a) as unpatentable over Guo, et al. in view of Sornasse et al. (1992).

The Office Action states that the previous arguments were not persuasive. Notably, regarding arguments directed to the unsuitability of spleen cells as a source of dendritic cells (DC) to produce dendritic cell/ tumor cell hybrids, the Office Action points out that the first six examples of the specification were produced using spleen cells. The Examiner posits that it is not clear how the source of the DC's render the claims patentably distinct but suggests that limitation of the claims to exclude splenic cells to be consistent with that position.

With this amendment, independent claim 1 has been amended as suggested above. That is, Claim 1 is limited to "dendritic cells from bone marrow, lymph or blood, or, preparing said dendritic cells by differentiating in vitro precursors isolated from bone marrow, lymph or blood", consistent with Applicants' position as presented in the last response. Applicants point out that while isolation of dendritic cells from bone marrow, blood and lymph was known at the time of the claimed invention, preparation of DC/ tumor cell hybrids from DCs derived from bone marrow, blood and lymph was not. Accordingly, as all of the claims depend ultimately from Claim 1, the claims as amended are believed to be patentable over the art of record.

Support for the amendment is found as follows. Support for the source of the dendritic cells is found in cancelled claims 19-20 & 47-50 as well as at paragraphs 0081, 0094-0099, and 0141 from the published application, US2001/0012632. Said paragraphs correspond to the following paragraphs of the priority document (08/414,480) p.12, l.16-29, p.14, l.20 to p.15, l.22

(in particular, p.14, l.21-24, p.15, l.1-3, l.6-8, l.12-14, l.18-19); and p.30, l.20 and l.28-29. Support for "proliferating" is found in paragraph 0184. Specific support for "not a T-lymphocyte or B-lymphocyte" is found in paragraph 0151, lines 19-22 and also in paragraph 0024.

Applicants have also rewritten Claim 3 as new Claim 52 in order to simplify and reduce the total number of claims. Support is found in cancelled Claim 3 and in the published application at paragraphs 0085 and 0086.

The presently claimed invention is clearly non-obvious over Guo, et al. as the B-cells of Guo, et al. are specifically excluded. Furthermore, Sornasse, et al. do not provide sufficient motivation to substitute dendritic cells for the B-cells taught by Guo, et al. In any case, neither Sornasse, et al nor Guo, et al. teach or suggest the importance of isolating DCs from a source rich in DC progenitors such as the recited bone marrow, blood or lymph at a time when the DCs are proliferating and are not yet at a mature stage as claimed. Clearly, the importance of the source used for isolation of DCs was not known at the time of the claimed invention as indicated also by the Examiner on page 5 of the last Office Action at paragraph 3.

It was previously argued that the production of DC/tumor hybrids was not predictable at the time of the claimed invention as discussed in the Declaration of Dr. Moser submitted with the previous response (hereafter Moser I). In the Moser I Declaration, Dr. Moser states that it could not have been predicted at the time of the claimed invention that replacing the B cells of Guo, et al. with DC cells would lead to the DC/tumor cell hybrids of the claimed invention because of observations at the time of the claimed invention that fusion of dissimilar cells often resulted in loss of expression of tissue specific traits. Thus, it was not predictable at the time of the claimed invention that DC /tumor cell hybrids (hybridomas) could be made which could be administered to produce an anti-tumor response as claimed. In addition, only based on the teaching of the present application (see examples 7-13 of the present application), may a skilled person predict that the production of said DC/tumor hybrids/hybridomas is feasible.
The present invention proves for the first time that the hybrids/hybridomas of the present invention allow the efficient elimination of tumors in animals.

As argued previously, while DCs may be present in spleen, it is not feasible to produce DC/tumor cell hybrids starting from spleen cells. This is illustrated in the present application (see examples 1-6 of the present application) and Guo et al. (1994). Both confirm that, when using

spleen cells, B-cell/tumor cell and T-cell/tumor cell hybrids are be formed, not DC/tumor cell hybrids. This was also argued previously in the Moser I Declaration (section 3).

The fact that proliferating DCs, derived from bone marrow, blood or lymph are a better alternative to spleen cells (used by Guo and Sornasse) to start the production of the hybrids of the present invention was taught in the '397 application as originally filed and published (in for instance paragraph 0184). The presently claimed invention allows a more efficient production of DC/tumor hybrids/hybridomas by using bone marrow, blood or lymph as a source of DCs.

The Office Action points out that the first six examples of the specification were produced using spleen cells. However, this is believed to further substantiate Applicants' position as these Examples did not result in successful DC/tumor cell fusions as discussed in the last response and repeated above. The result was a T-cell/tumor cell hybrid, not a DC/tumor cell hybrid.

As previously discussed, spleen cells do not contain proliferating (differentiating) cells, or they are present in a negligible amount. This is consistent with the specification which shows that spleen cells are not a good choice for isolation of DC to make DC/tumor cell fusions (see paragraph 0184 of the published application). This was not known at the time of the invention which is why the initial experiments were performed (unsuccessfully) using spleen cells. The successful use of other sources such as bone marrow, lymph or blood is shown by the present specification and is the focus of the present claims.

Applicants present a second Declaration of Dr. Moser (hereafter Moser II) which provides additional data which corroborates the statements made above. DCs were isolated at different culture times, characterized and used in fusion experiments. The work confirms the conclusion in the present specification that proliferating, less differentiated DCs, and in particular those derived from bone marrow, blood and lymph, may be used significantly more effectively in DC/tumor cell fusions.

As discussed in paragraph 9 of the Moser II Declaration, spleen and lymph nodes contain a high proportion of differentiated DCs. These make poor fusion partners. This was not known by others at the time of the claimed invention but was discovered by the present inventors and is clearly shown in the specification. Examples 1-6 of the present specification demonstrate that DC/tumor cell hybrids could not be produced using spleen as the DC source. See also paragraph 0184 of the published application. In contrast when blood is used as the source (Examples 8-11),

differentiating DCs are obtained and used for a monocyte/tumor cell fusion. This fusion represents a fusion partner which is intermediate between a monocyte and a DC, albeit with more features of a monocyte (see paras. 0150-0152 of the published application). In Example 12, bone marrow was used to isolate differentiating DCs and a DC/tumor cell hybrid was obtained.

The use of bone marrow, lymph or blood as the DC source as now claimed has the further advantage that it is possible to obtain the source material using minimally invasive procedures. The use of an autologous source as set forth in new claim 51 has advantages in peace of mind for the patient concerned about tissue and blood borne diseases such as AIDS, mad cow disease and West Nile virus.

In view of Applicants' submitted Declarations, arguments and amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Claims 5-10, 38, and 46 are rejected under 35 U.S.C. § 103 (a) as unpatentable over Guo, et al. in view of Sornasse, et al. as applied to Claims 1, 3, and 19-26 above and further in view of U.S. Patent No. 5,851,756 for reasons of record as set forth in the action mailed 8/12/03.

This ground of rejection is moot with respect to claims 6, 8, 10, and 46 as those claims have been cancelled. With respect to claims 5, 7, 9, and 38, Applicants again argue that before the filing date of the present application, it was not clear that DC characteristics could be further induced in DC/ tumor cell fusions. The '756 patent relates to the use of GM-CSF to increase the number of DC cells and only relates to non-fused DCs. The '756 disclosure does not teach that DC characteristics could be induced. Furthermore, there is no teaching on induction of any kind of DC/tumor cell fusions. Accordingly, the combination of references does not teach induction of any kind as recited in claims 5 and 7 or specifically using GM-CSF as recited in claim 9.

Furthermore, since claims 5, 7, 9, and 38 depend ultimately from Claim 1, which is neither taught nor suggested by the cited references, the invention defined in claim 5, 7, 9, and 38 is also patentably distinguished from the references, alone or in combination.

Applicants respectfully request the withdrawal of the rejection.

Claims 11-18 are rejected under 35 U.S.C. § 103 (a) as unpatentable over Guo, et al. in view of Sornasse, et al. as applied to Claims 1, 3, and 19-26 above and further in view of U.S. Patent No. 5,637,483 for the reasons of record as set forth in the action mailed 8/12/03.

This ground of rejection is moot with respect to claims 12, 14, 16, and 18 as these claims have been cancelled. As claims 11, 13, 15 and 17 depend from claim 1, which is neither taught

nor suggested by the cited references as discussed above, the invention defined in claims 11, 13, 15 and 17 is also patentably distinguished from the references, alone or in combination. Applicants respectfully request the withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 5-24, and 29-50 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) has possession of the claimed invention at the time that the application was filed.

Regarding Part A of this ground of rejection, the Examiner asserts that there is no support for the recitation of "wherein said dendritic cell is not a T-lymphocyte, B-lymphocyte, monocyte/macrophage or another non-dendritic cell present in enriched or purified dendritic cell preparations" in claims 1 and 3. Without acquiescing to this ground of rejection, Claim 1 has been amended to recite "wherein said dendritic cell is not a T-lymphocyte or B-lymphocyte". Support for this amendment may be found specifically in paragraph 0151, lines 19-22 and also in paragraph 0024. Claim 3 has been cancelled and replaced by Claim 52 which depends from Claim 1 as discussed above.

Part "B" of this ground of rejection is moot as claims 35, 43, 48 and 50 have been cancelled.

In view of Applicants amendments and arguments, withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 31-46 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This ground of rejection is moot in view of Applicants' cancellation of claims 31-37, 39-46, and amendment of claim 38. Withdrawal is requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the

application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Feb. 4, 2005

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